Who will benefit from uterus-sparing surgery in adenomyosis-associated subfertility?

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Objective: To analyze the determinants of successful pregnancy following laparoscopic adenomyomectomy.
Design: Retrospective cohort study.
Setting: A general hospital.
Patient(s): A total of 102 women who had a desire for pregnancy underwent laparoscopic adenomyomectomy from 2007 to 2012.
Intervention(s): Surgical excision of the uterine adenomyosis; statistical analysis for fertility outcomes.
Main Outcome Measure(s): Pregnancy rates and the results of univariable and multivariable analyses.
Result(s): When the women were divided into ≤39 years and ≥40 years age groups, clinical pregnancy rates were 41.3% and 3.7%, respectively. Factors associated with clinical pregnancy were: history of IVF treatments, posterior wall involvements, and age, with odds ratios of 6.22, 0.18, and 0.77, respectively. In the younger group, 60.8% of women with history of IVF failure showed successful pregnancy after surgery. We experienced 2 cases of placenta accreta in far advanced cases.
Conclusion(s): This study demonstrated age as a determinant in fertility outcomes. Surgery could be a beneficial treatment for women who experienced IVF treatment failures, especially at ages of ≤39 years. We could not show a clear benefit of the surgery on fertility outcomes of the group aged ≥40 years. Extremely severe adenomyosis affecting a broad range of the uterine subendomerial myometrium should be treated carefully on a pregnancy course. (Fertil Steril® 2014;102:802–7. ©2014 by American Society for Reproductive Medicine.)
Key Words: Adenomyosis, surgery, subfertility, pregnancy, complication

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Uterine adenomyosis is defined by the presence of endometrial glands and stroma surrounded by the hypertrophic and hyperplasic myometrium (1), and its pathogenesis is still not explained sufficiently. Generally, adenomyosis is accepted to result from a direct invasion of the endometrium into the myometrium, and is thought to be found most likely during the fourth and fifth decades of life and after childbearing activity. However, with the trend of delayed childbearing, adenomyosis has come to be diagnosed more frequently in fertility clinics (2, 3). This is also thought to be caused by the recent development of diagnostic tools such as high-resolution transvaginal sonography and magnetic resonance imaging (MRI). With the aid of these diagnostic tools, uterine adenomyosis is becoming a more common disease among women with childbearing desire and showing more diversity (4–9). Recently, the correlation between adenomyosis and endometriosis has gradually been revealed (4–9). We often encounter uterine adenomyosis without junctional zone (JZ) changes. This atypical adenomyosis often coexists with severe endometriosis and is localized at the outer myometrium without aberrations of the subendometrial myometrium (5, 7, 9).

Major treatment options for women wishing to preserve their fertility are thought to be assisted reproductive technologies (ART) and surgical removal of the adenomyosis. The impact of adenomyosis on in vitro fertilization (IVF) treatment outcomes is controversial (10–14). Two studies showed a positive effect of prolonged down-regulation on IVF outcomes of women with adenomyosis (10, 11), whereas another study reported a negative effect of adenomyosis on the final outcome of IVF treatment (12–14). Regarding surgical removal of adenomyosis, a recent review concluded that uterus-sparing surgery for adenomyosis appears to be feasible and satisfactory although pointing out the need of prospective well designed

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studies (15). At this stage, the true impact of various treatments on fertility outcomes of adenomyosis-associated subfertility has not been fully clarified (16).

We have applied laparoscopic excision surgery of the adenomyosis to symptomatic uterine adenomyosis, and among these cases roughly 72% of the women desired postoperative pregnancy. In the present study, we aimed to compile pregnancy outcomes following uterus-sparing surgery, and analyzed the determining factors of successful pregnancy. Furthermore, to the best of our knowledge, there is no study that has analyzed postoperative pregnancy outcomes in terms of the difference in localization of uterine adenomyosis. We also tried to incorporate this factor into the analysis of fertility outcomes.

MATERIALS AND METHODS

We retrospectively compiled the data of 141 women who underwent uterus-sparing surgery for uterine adenomyosis from April 2007 to December 2012 at the Department of Obstetrics and Gynecology, Takanohara Central Hospital, Nara, Japan. Among them, 102 had the desire for pregnancy at the time of surgery. Surgical and patient background data were retrieved from our surgical and patient database. Pregnancy outcomes were collected from questionnaires or interviews of outpatients. The median follow-up period was 24 months (range 9–60 months). We defined "clinical pregnancy" as the presence of a fetal heart beat at 12 weeks of gestation. All adenomyosis was diagnosed by preoperative MRI. The criteria used for the definition of adenomyosis on MRI were: 1) a myometrial mass with indistinct margins of primarily low intensity with all sequences; or 2) diffuse or local widening of the junctional zone on T2-weighted images (>12 mm) (17–19). All the adenomyosis cases were confirmed histologically. In the analysis of determining factors for clinical pregnancy, we used a univariable analysis and a multivariable regression analysis. In these analyses, we used the following variables: age at surgery, coexisting endometriosis, coexisting ovarian endometrioma, Revised American Fertility Society (r-AFS) scores, anterior wall involvements, posterior wall involvements, history of IVF treatments, weight of adenomyotic nodule, presence of JZ change in MR imaging. There was one missing piece of data. We couldn't follow one patient who was categorized as ≥40 years old, and the patient's pregnancy outcome was treated as "not pregnant." This study was approved by the Institutional Ethical Committee, and informed consent was obtained from each of the patients.

Statistical Analysis

The χ^2 test was used for the comparison of groups regarding categoric variables; the Fisher exact test was used in the case of small cell counts. Parametric and nonparametric continuous variables were compared with the use of the Student *t* test, and the Mann-Whitney *U* test was applied when the variables did not pass the normality test. *P* values of $<.05$ were considered to be statistically significant. Stepwise logistic regression analysis was used for the analysis of the factors related to clinical pregnancy (IBM statistics software, version 16; SPSS).

Surgical Procedures

The patient was placed in Trendelenburg position and triple puncture laparoscopic surgery performed. We initiated surgery by observation of the pelvic cavity to diagnose associated disorders. In cases having severe rectovaginal endometriosis, causing posterior cul-de-sac obliteration, we initiated the procedure by excision of the rectal endometriotic nodules from the anterior rectal wall, keeping the rectal endometriotic nodules attached to the posterior wall of the uterus; the excised nodules are removed en bloc with the posterior wall adenomyosis foci. After these preparations, we confirmed the boundary between the adenomyosis foci and healthy uterine myometrium to determine the extent of resection. An incision was made to the healthy myometrium just adjacent to the adenomyosis foci with the use of a potassium titanyl phosphate laser. The incision was performed step by step by making traction between the adenomyosis foci and the healthy muscles; the difference between the adenomyotic nodule and healthy muscles could be distinguished by the difference in extensibility. Adenomyosis tissues are less elastic than the normal uterine muscles because of fibrotic changes. However, because the border is unclear, we made incision to the healthy uterine muscles just adjacent to the adenomyosis foci. In this way, we remove the adenomyosis foci en bloc as completely as possible. After removal of the adenomyosis foci, the defected spaces were carefully repaired with continuous stitches of 2-0 synthetic absorbable sutures to close the residual myometrium.

RESULTS

Patients' Backgrounds and Surgical Data

Background aspects of the 102 women who had a desire for pregnancy are summarized in Table 1. When the women were divided into ≤39 and ≥40 years age groups, significant differences were found in the number of years of infertile and percentages of women who had coexisting endometriosis. There was no significant difference in stages of endometriosis or r-AFS scores. The weight of adenomyotic nodules of the older age group was relatively heavier than that of the younger group (not significantly); however, blood loss and the open conversion rate of the older group were significantly higher.

Pregnancy Outcomes

Pregnancy outcomes are presented in Table 2. The clinical pregnancy rate was totally 31.4% (32/102). When the women were divided into ≤39 and ≥40 years, clinical pregnancy rates were 41.3% and 3.7%, respectively. In the older group, 5/6 of the pregnancies ended in miscarriages. All of the women who succeeded in clinical pregnancy were delivered with the use of elective cesarean section. Next, we analyzed fertility outcomes on women who had a history of IVF failures. In the younger group, 60.8% of the women succeeded in postoperative clinical pregnancy. In contrast, the clinical pregnancy rate of the older group was 7.1%. Most of the women had successful pregnancies with the use of IVF